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Selective reduction of condensed *N*-heterocycles using water as a solvent and a hydrogen source

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The reduction of unprotected indoles and quinolines is described using water as a hydrogen source. The method is based on the application of a RANEY® type Ni–Al alloy in an aqueous medium. During the reaction the Al content of the alloy, used as reductants, reacts with water *in situ* providing hydrogen and a RANEY® Ni catalyst, thus the alloy serves as a hydrogen generator as well as a hydrogenation catalyst. The simplicity and efficacy of the method are illustrated by the selective reduction of a variety of substituted indoles and quinolines to indolines and tetrahydroquinolines, respectively.

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Introduction

Reduction of functional groups is a fundamental transformation in synthetic organic chemistry.[1] Due to the large variety of organic compounds a broad array of reduction methods were described.[2] The focus of recent developments is the use of safe and convenient reagents and solvents to address the ever growing concern of safety and sustainability and to minimize or, preferably, eliminate waste.[3]

Hydrogenation of *N*-heterocycles is a difficult task due to the highly resonance stabilized aromatic nucleus.[4] The fact that the product secondary amine could act as a poison to most industrially common heterogeneous metal catalysts represents another major problem.[5] The products can also undergo further hydrogenation to form by products up to perhydrogenated compounds. Extended efforts have been devoted to the selective hydrogenation of these compounds, particularly indoles and quinolines. Since Paul Sabatier's pioneering work on Ni-catalyzed hydrogenations,[6] heterogeneous catalytic hydrogenation[7] has become one of the longest known procedures in organic synthesis. The selective reduction of *N*-heterocycles, however, still presents a challenge due to a multitude of problems.[8] Several protocols were developed for the reduction of indoles[9] and quinolines[10] by stoichiometric methods. While being effective, these methods have selectivity problems.[11] Homogeneous catalytic methods for the hydrogenation of N-protected indoles[12–14] or quinolines[15] were also reported. Heterogeneous catalysts have been used for the hydrogenation of these heterocycles.[16] Despite some progress the reports are mostly limited to N-protected indoles.[17] The reduction of unprotected indoles by heterogeneous catalytic hydrogenation using hydrogen gas requires harsh conditions (H_2 pressure of 150 bar, T of 227 °C).[18]

In a recent work we described a new acid-assisted heterogeneous catalytic hydrogenation for the selective reduction of unprotected indoles partially solving the problem.[19]

The heterogeneous catalytic hydrogenation of quinolines also attracted attention, although the number of practical examples are limited.[20] Expanding on our interest in developing new environmentally benign synthetic methologies,[21] we explored the application of the aqueous Ni–Al alloy hydrogenation system in which hydrogen is generated *in situ*.[22] With the rise of the green or sustainable chemistry concept,[23] considering water as a possible solvent or reagent attracts great attention in organic synthesis.[24] In the field of reductions, water was also used as a solvent for example in the hydrogenation of C=N double bonds catalyzed by cyclodextrin-stabilized Pd nanoparticles.[25] The application of the Ni–Al and various other transition metal–Al alloys (Co, Cu, Fe) in dilute alkaline aqueous solution was introduced and pioneered by Tashiro and Fukata for the reduction of aryl ketones, phenols, naphthalenes, biphenyls, acenaphthene and benzophenones or several dehalogenation reactions.[26] While our current work builds on the beforementioned preliminaries our combined use of ultrasonic irradiation and alkali-free aqueous medium resulted in a *tamed* Ni–Al alloy, which allowed for the more selective reductions of heterocycles.

Herein we describe the selective reduction of unprotected indoles and quinolines in water using a nickel–aluminium

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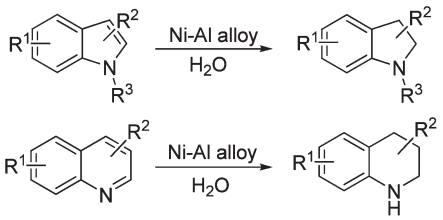


Scheme 1 Selective reduction of indoles and quinolines in water by a Ni–Al alloy.

alloy (Scheme 1). The products indolines and tetrahydroquinolines are biologically active compounds of pharmaceutical importance.[27]

Results and discussion

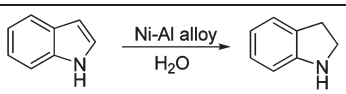
The selective reduction of indole as a highly activated aromatic compound is particularly difficult; the presence of even weak electrophiles initiates polymerization.[28] The other problem is overhydrogenation, mainly to octahydroindole. Due to the formation of $Al(OH)_3$ in the present reaction, the pH of the system will be basic and it was expected that earlier problems, such as polymerization, can be avoided. Thus, first the effect of the reaction conditions on the yield and selectivity was assessed using the hydrogenation of indole as a test reaction (Table 1).

Based on our experience in handling of Ni–Al initiated reductions[22] a broad variety of parameters, such as temperature, reaction time and activation method, were tested. The data in Table 1 reveal some major characteristics of the reduction. While the aluminium content of the Ni–Al alloy reacts at ambient temperature, it shows a significant lag-phase and provides near complete conversion only after 72 h (entries 1–3).

The selectivity is 100% at low conversion, but after longer reaction times and higher conversion selectivity drops to 65% indicating the formation of, mainly overhydrogenated, by-products. Higher temperature resulted in more rapid reaction, while maintaining high selectivity (entry 4). The application of microwave irradiation at the same temperature did not result in major improvement (entry 5). Interestingly, ultrasonic activation appeared to be an effective method with good initial yield and excellent selectivity (entry 6), however, the increased reaction times only yielded minor improvement in the conversion (entry 7). Nevertheless, these experiments (entries 6 and 7) indicated that ultrasounds had a beneficial effect on the reaction that could be, at least in part, explained by the well-known surface cleaning effect of ultrasonic waves.[29]

Since the *in situ* generation of hydrogen is a crucial part of the reaction mechanism, a clean, oxide-free aluminium surface is of utmost importance. The removal of the surface Al_2O_3 layer shortens the induction period and results in rapid reaction rates (entry 4 *vs.* 12). In addition, the presonication of metal catalysts results in smaller particle size, thus a greater surface area for the remaining metal (Ni), which, in our experience, improves reaction rates.[30] It was also observed that longer sonochemical pretreatment resulted in lower yields (entries 13 and 14). This phenomenon is most likely due to the partial dissolution of the Al content of the alloy, thus reducing the amount of hydrogen generated for the subsequent reaction. It appears that a 1 h presonication improves the performance by surface cleaning and particle size reduction, however, the excessive consumption of the hydrogen source (Al) upon oversonication of the alloy decreases the yield. Based on the data above, it was concluded that 1 h presonication combined with conventional heating at 50 °C are the best parameters for the reaction.

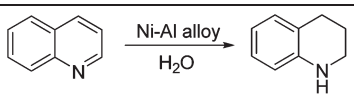
Table 1 Effect of experimental parameters on the synthesis of indoline *via* the reduction of indole by a Ni–Al/H_2O system[a]



Entry	Method[b]	*T* [°C]	Time [h]	Conv.[c] [%]	Sel.[c] [%]
1	CH	25	24	0	0
2	CH	25	48	3	100
3	CH	25	72	96	65
4	CH	110	3	54	93
5	MW	110	2	54	100
6	US	25	1	43	100
7	US	25	2	58	100
8	1 h preUS, CH	25	24	74	77
9	1 h preUS, CH	25	48	97	72
10	1 h preUS, CH	25	72	84	77
11	1 h preUS, CH[d]	50	24	83	100
12	1 h preUS, CH	110	3	93	91
13	2 h preUS, CH	110	3	80	95
14	2 h preUS, MW	110	1	74	100

[a] Reactions were carried out with 200 mg Ni–Al, 3 mL water, 0.34 mmol indole. [b] CH, conventional heating; MW, microwave irradiation; US, ultrasonic irradiation; preUS, presonication of the alloy only. [c] Conversion and selectivity were determined by GC. [d] The presonication was carried out in the presence of indole.

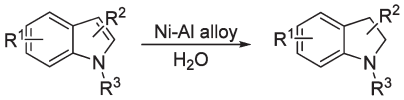
Table 2 Effect of experimental parameters on the synthesis of tetrahydroquinoline *via* the reduction of quinoline by a Ni–Al/H_2O system[a]



Entry	Method[b]	*T* [°C]	Time [h]	Conv.[c] [%]	Sel.[c] [%]
1	1 h preUS, CH	25	24	32	65
2	1 h preUS, CH	110	3	97	80
3	1 h preUS, CH	110	1	93	90
4	1 h preUS, MW	110	1	100	93

[a] Reactions were carried out with 1 h presonicated 200 mg Ni–Al, 3 mL water, 0.31 mmol quinoline. [b] CH, conventional heating; MW, microwave irradiation; US, ultrasonic irradiation; preUS, presonication of the alloy only. [c] Conversion and selectivity were determined by GC.

Table 3 Synthesis of indolines *via* the reduction of indoles by a Ni–Al/H_2O system[a]



Entry	R^1	R^2	R^3	Method	T [°C]	Time [h]	Yield[b,c] [%]
1	H	H	H	B	50	24	83
2	H	H	CH_3	A	25	24	79
3	5-CH_3	H	H	B	80	8	77
4	7-CH_3	H	H	B	80	8	84
5	5-CO_2CH_3	H	H	A	25	48	70
6	7-C_2H_5	H	H	A	25	3	73[c]
7	5-OCH_3	H	H	A	25	24	78
8	4,6-Di-(OCH_3)	3-CH_3	H	B	50	42	68

[a] Method A: 200 mg Ni–Al, presonicated for 1 h in 3 mL water, then 0.34 mmol indole. Method B: 200 mg Ni–Al, sonicated for 1 h in 3 mL water with 0.34 mmol indole then stirred for the required time. [b] GC yields. [c] The reaction was carried out with continuous sonication.

Table 4 Synthesis of tetrahydroquinolines *via* the reduction of quinolines by a Ni–Al/H_2O system[a]

Entry	R^1	R^2	T [°C]	Time [h]	Yield[b] [%]
1	H	H	110	1	92
2	6-CH_3	H	110	1	93
3	6-OCH_3	H	110	1	97
4	7-CH_3	H	110	1	99
5	8-CH_3	H	110	1	92
6	6-CH_3	2-CH_3	110	1	95
7	H	3-CH_3	110	2	72
8	H (isoquinoline)	H	150	2	81

[a] Reactions were carried out with 200 mg Ni–Al, 3 mL water, 0.34 mmol quinoline; MW, microwave irradiation; preUS, presonication of the alloy only. [b] GC yields.

As our goal was to extend the method to other condensed *N*-heterocycles, the reduction of quinoline was studied (Table 2) mainly under the previously optimized conditions.

Due to the positive effect of presonication on the reduction of indole this method was further optimized for quinoline. Table 2 indicates that these conditions work well for quinoline as well. The only major change is that in this reduction the microwave heating provided the best conversion and selectivity, thus better overall yield. Therefore, these conditions (entry 4) were selected for further investigations of quinolines.

After identifying the optimum reaction conditions for our test substrates, efforts were made to further explore the scope of this reduction method. We uniformly adopted the use of the 1 h ultrasonic pretreatment that largely eliminated the lag phase of the reaction. The data obtained with several substituted indoles are summarized in Table 3.

As shown (Table 3), a variety of substituted indoles were hydrogenated to the corresponding indolines in good yields. It was observed, however, that the substituted indoles showed stronger sensitivity than that of an unsubstituted indole (Table 1). Thus, further optimization was carried out with these compounds and the data in Table 3 reflect the best conditions found. Several reactions were carried out at room temperature due to the low selectivity values observed at higher temperatures.

Similarly to indoles, the scope of the reduction was also investigated using a variety of quinoline derivatives. The data are tabulated in Table 4.

As the data in Table 4 indicate that the yields of quinoline reduction are generally about 10% higher than that of indoline synthesis (Table 3). The improved yields are most likely due to the significantly lower reactivity of the quinoline moiety, which makes it resistant toward secondary reactions and allows the application of higher temperatures. While the conversion in the hydrogenation of indoles also increases with temperature so does the amount of by-products, which decreases the overall yield in high temperature reactions.

The key step in the reaction mechanism involves the reaction of the Al content of the alloy in water, which is used as a reductant and generates the hydrogen necessary for the reduction. The Al_2O_3 layer that commonly forms on the surface of Al makes this process extremely slow as shown by the long lag-period in Table 1 (entries 1–3).

This long induction period can significantly be reduced by the addition of a base that would also improve the dissolution rate of aluminium.[24] The presence of a base, however, often caused selectivity problems, mainly significant and uncontrollable overhydrogenation.[24] Since selectivity is an important issue here, especially in the case of indoles, we decided to avoid the use of a base, in order to tame the reduction system, as well as to keep it as *green* as possible. Thus, we opted for the use of a physical surface cleaning method and applied ultrasonic irradiation in the form of a bath. Bath-type sonicators are known to work better under heterogeneous conditions[26,27] such as the target reaction in this work. While ultrasounds exposed the Al surface to the aqueous medium the lack of a base resulted in the evolution of hydrogen at a moderate rate, which helped to avoid undesired side reactions, most commonly overhydrogenation. The presence of Ni, an active, hydrogenation capable transition metal ensures the appropriate and rapid use of the hydrogen formed. The flow of the reaction is illustrated in Fig. 1.

As compared to other "dissolving metal" type reductions the current process carries several advantages, most of which are related to the use of the Ni–Al alloy.

(i) The reaction can be carried out with unprotected indoles, which eliminates the protection and deprotection steps required in earlier reports and the losses of product and waste formation associated with these steps. (ii) The reaction is carried out in neat water, a benign, readily available and

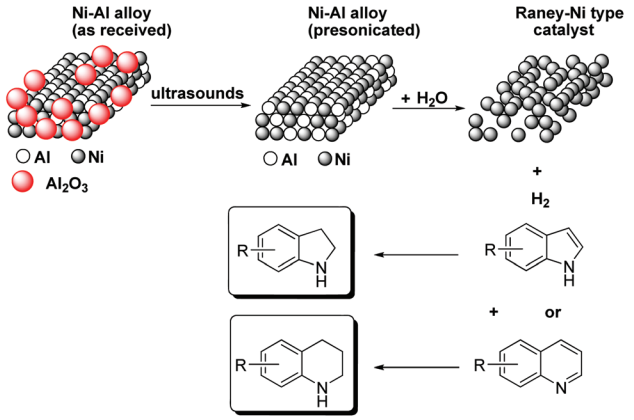


Fig. 1 Reduction of indoles and quinolines by a presonicated Ni–Al alloy in water.

inexpensive solvent without the use of any other chemicals (acids or bases). It must be mentioned, however, that an organic solvent, ethyl acetate, was used to extract the products from the aqueous medium, thus adding an organic solvent to the process. The combined use of ultrasounds and alkali-free aqueous medium significantly moderates the Ni–Al alloy and, in general, allows obtaining selectivities much higher than those described in earlier studies that used NaOH and similar solutions. The reduction in activity is indicated by slower and more controlled H_2 formation, which decreases the potential hazards associated with reductive agents; (iii) due to the controlled rate of hydrogen formation the selectivity is high; (iv) the use of aluminium as a reductant makes the reaction simple and safe, one does not have to face the safety and environmental problems associated with the use of Na or Zn/Hg; (v) the Ni content of the alloy forms a RANEY® Ni type hydrogenation catalyst that adsorbs hydrogen readily and ensures the economic use of the alloy as well as the effective hydrogenation of the substrates; (vi) considering all of the above, the reaction does not generate harmful waste. The only by-product that forms is an alumina supported Ni catalyst (Ni/Al_2O_3) that could be filtered and used in other hydrogenation processes.

Conclusions

In summary, a Ni–Al alloy induced reduction methodology was developed for the synthesis of indolines and tetrahydroquinolines from unprotected indoles and quinolines using aluminium as a reductant and water as a solvent as well as a hydrogen source. The reactions were carried out in a simple setting and under mild conditions. Products were obtained in good to excellent yields and high selectivities. The method, with its effective, inexpensive, simple and selective design provides a convenient solution for the reduction of indoles and quinolines and most likely can be extended to the reduction of a broad range of substrates.

Experimental

General information

All indoles, quinolines and the Al–Ni alloy (50% Al–50% Ni) were purchased from Sigma-Aldrich and used without further purification. Solvents used in synthesis were of minimum purity of 99.5% and were purchased from Thermo Fisher Scientific. Water used as a solvent in the reactions was deionized water. The mass spectrometric identification of the products has been carried out by an Agilent 6850 gas chromatograph-5973 mass spectrometer system (70 eV electron impact ionization) using a 30 m long DB-5 type column (J&W Scientific). The ^1H and ^{13}C spectra were obtained on a 300 MHz Varian NMR spectrometer, in $CDCl_3$ using tetramethylsilane or the residual solvent signal for reference. The temperature was 25 °C (accuracy ± 1 °C) and controlled by the Varian control unit.

Representative procedures for the reduction of indoles to indolines

Procedure A. Al–Ni alloy (200 mg) was suspended in 3 mL of deionized water and sonicated (Branson 1510MTH ultrasonic bath) for 1 h. Then, indole (40 mg, 0.34 mmol) was added to the preactivated alloy. The reaction mixture was stirred for 3 h at 110 °C. After the completion of the reaction, the alloy was removed by filtration. The filtrate was extracted with two portions of 2 mL of ethyl acetate (EtOAc). The organic extracts were combined and dried over Na_2SO_4. The solvent was removed in a vacuum and the crude product was purified by flash chromatography.

Procedure B. Al–Ni alloy (200 mg) and indole (40 mg, 0.34 mmol) were suspended in 3 mL of deionized water and sonicated (Branson 1510MTH ultrasonic bath) for 1 h. Then, the reaction mixture was stirred for 24 h at 50 °C. After the completion of the reaction, the alloy was removed by filtration. The filtrate was extracted with two portions of 2 mL of EtOAc. The organic extracts were combined and dried over Na_2SO_4. The solvent was removed in a vacuum and the crude product was purified by flash chromatography.

Representative procedure for the reduction of quinoline to tetrahydroquinoline

Al–Ni alloy (200 mg) was suspended in 3 mL of deionized water and sonicated (Branson 1510MTH ultrasonic bath) for 1 h. Then, the mixture was transferred into a microwave reaction tube and quinoline (40 mg, 0.31 mmol) was added to the preactivated alloy. The reaction mixture was stirred for 1 h at 110 °C in a CEM Discover microwave reactor. After the completion of the reaction, the alloy was removed by filtration. The filtrate was extracted with two portions of 2 mL of EtOAc. The organic extracts were combined and dried over Na_2SO_4. The solvent was removed in a vacuum and the crude product was purified by flash chromatography.

The compounds are known in the literature[10,19] and their spectra are in good correlation with previous reports. The spectral characterization of the products is given below.

Indoline (Table 3, entry 1). Colorless oil, R_f = 0.30 (20% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.21 (d, J = 7.2 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 6.80 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 3.59 (t, J = 8.4 Hz, 2H), 3.10 (t, J = 8.1 Hz, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 151.4, 129.1, 126.9, 124.4, 118.4, 109.2, 47.1, 29.6; **MS**-C_8H_9N (119) m/z (%): 119 (M^+, 100), 91 (21), 77 (2), 65 (6), 58 (7).

1-Methylindoline (Table 3, entry 2). Brown oil, R_f = 0.25 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.07 (m, 2H), 6.66 (t, J = 7.5 Hz, 1H), 6.48 (d, J = 8.1 Hz, 1H), 3.27 (t, J = 8.4 Hz, 2H), 2.92 (t, J = 8.4 Hz, 2H), 2.74 (s, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 153.3, 130.2, 127.2, 124.1, 117.6, 107.1, 56.0, 36.2, 28.6; **MS**-$C_9H_{11}N$ (133) m/z (%): 133 (M^+, 100), 117 (41), 103 (4), 91 (10), 77 (6).

5-Methylindoline (Table 3, entry 3). Light brown oil, R_f = 0.25 (20% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.93 (s, 1H), 6.80 (d, J = 7.8 Hz, 1H), 6.52 (d, J = 7.5 Hz, 1H), 3.47 (t, J = 8.1 Hz, 2H), 2.95 (t, J = 8.1 Hz, 2H), 2.23 (s, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 149.4, 129.9, 128.2, 127.7, 125.6, 109.6, 47.8, 30.2, 21.0; **MS**-$C_9H_{11}N$ (133) m/z (%): 133 (M^+, 100), 117 (28), 103 (5), 77 (9), 65 (7).

7-Methylindoline (Table 3, entry 4). Light brown oil, R_f = 0.30 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.99 (d, J = 6.0 Hz, 1H), 6.87 (d, J = 9.0 Hz, 1H), 6.66 (t, J = 6.0 Hz, 1H), 3.56 (t, J = 9.0 Hz, 2H), 3.05 (t, J = 9.0 Hz, 2H), 2.13 (s, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 150.0, 128.6, 128.1, 122.1, 118.9, 118.8, 47.2, 30.1, 16.8; **MS**-$C_9H_{11}N$ (133) m/z (%): 132 (M^+, 100), 117 (42), 103 (6), 77 (9), 65 (7).

Methyl indoline-5-carboxylate (Table 3, entry 5). Light orange solid, R_f = 0.20 (20% EtOAc in hexane); **M.P.**: 67–69 °C; **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.76 (m, 2H), 6.55 (d, J = 8.4 Hz, 1H), 3.84 (s, 3H), 3.65 (t, J = 8.4 Hz, 2H), 3.07 (t, J = 8.4 Hz, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 125.9, 199.4, 130.7, 128.7, 126.1, 107.4, 100.0, 51.6, 47.3, 28.8; **MS**-$C_{10}H_{11}NO_2$ (177) m/z (%): 177 (M^+, 82), 146 (100), 118 (27), 89 (12), 72 (6).

7-Ethylindoline (Table 3, entry 6). Brown oil, R_f = 0.33 (20% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.90 (d, J = 7.2 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.79 (t, J = 7.5 Hz, 1H), 3.63 (t, J = 8.1 Hz, 2H), 3.55 (bs, 1H), 3.12 (t, J = 8.4 Hz, 2H), 2.56 (q, J = 7.5 Hz, 2H), 1.31 (t, J = 7.5 Hz, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 149.3, 128.7, 125.9, 124.8, 122.0, 118.8, 47.1, 29.9, 24.0, 13.1; **MS**-$C_{10}H_{13}N$ (147) m/z (%): 147 (M^+, 63), 132 (100), 117 (24), 105 (7), 91 (6).

5-Methoxyindoline (Table 3, entry 7). Light brown oil, R_f = 0.25 (30% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.78 (s, 1H), 6.60 (m, 2H), 3.75 (s, 3H), 3.50 (t, J = 8.4 Hz, 2H), 3.00 (t, J = 8.1 Hz, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 153.6, 145.5, 131.3, 112.2, 111.6, 110.2, 56.0, 47.9, 30.6; **MS**-$C_9H_{11}NO$ (149) m/z (%): 149 (M^+, 54), 134 (100), 117 (3), 104 (9), 77 (7).

4,6-Dimethoxy-3-methylindoline (Table 3, entry 8). Light brown oil, R_f = 0.25 (20% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 5.90 (m, 2H), 3.76 (d, J = 9.9 Hz, 6H), 3.70 (t, J = 8.7 Hz, 1H), 3.38 (m, 1H), 3.14 (dd, J = 8.7, 5.1, 1H), 1.26 (d, J = 6.6 Hz, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 161.2, 157.0, 153.1, 112.8, 89.3, 88.6, 55.5, 55.3, 55.0, 34.5, 19.0; **MS**-$C_{11}H_{15}NO_2$ (193) m/z (%): 193 (M^+, 38), 178 (100), 163 (18), 147 (20), 132 (7).

Tetrahydroquinoline (Table 4, entry 1). Yellow oil, R_f = 0.34 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.00 (m, 2H), 6.65 (t, J = 6.0 Hz, 1H), 6.50 (d, J = 6.0 Hz, 1H), 3.32 (t, J = 6.0 Hz, 2H), 2.80 (t, J = 6.0 Hz, 2H), 1.98 (m, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 144.7, 129.4, 126.6, 121.3, 116.8, 114.1, 41.9, 26.9, 22.1; **MS**-$C_9H_{11}N$ (133) m/z (%): 132 (M^+, 100), 118 (21), 104 (8), 77 (10).

6-Methyl-tetrahydroquinoline (Table 4, entry 2). Light yellow oil, R_f = 0.32 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.70 (s, 2H), 6.33 (d, J = 9.0 Hz, 1H), 3.18 (t, J = 6.0 Hz, 2H), 2.65 (t, J = 6.0 Hz, 2H), 2.12 (s, 3H), 1.85 (m, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 142.3, 130.0, 127.2, 126.2, 121.5, 114.4, 42.1, 26.8, 22.4, 20.4; **MS**-$C_{10}H_{13}N$ (147) m/z (%): 146 (M^+, 100), 132 (34), 117 (17), 91(12).

6-Methoxy-tetrahydroquinoline (Table 4, entry 3). Light yellow oil, R_f = 0.16 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.51 (m, 2H), 6.38 (d, J = 9.0 Hz, 1H), 3.65 (s, 3H), 3.17 (t, J = 6.0 Hz, 2H), 2.67 (t, J = 6.0 Hz, 2H), 1.85 (m, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 151.8, 138.7, 122.9, 115.6, 114.8, 112.8, 55.7, 42.3, 27.1 22.4; **MS**-$C_{10}H_{13}NO$ (163) m/z (%): 163 (M^+, 51), 148 (100), 130 (5), 118 (7).

7-Methyl-tetrahydroquinoline (Table 4, entry 4). Light yellow oil, R_f = 0.34 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.80 (d, J = 6.0 Hz, 1H), 6.40 (d, J = 6.0 Hz, 1H), 6.26 (s, 1H), 3.23 (t, J = 6.0 Hz, 2H), 2.68 (t, J = 6.0 Hz, 2H), 2.18 (s, 3H), 1.88 (m, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 144.5, 136.3, 129.3, 118.5, 117.8, 114.7, 41.9, 26.5, 22.3, 21.1; **MS**-$C_{10}H_{13}N$ (147) m/z (%): 147 (M^+, 100), 132 (53), 117 (20), 91 (13).

8-Methyl-tetrahydroquinoline (Table 4, entry 5). Light yellow oil, R_f = 0.39 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.77 (t, J = 6.0 Hz, 2H), 6.47 (t, J = 6.0 Hz, 1H), 3.28 (t, J = 6.0 Hz, 2H), 2.70 (m, 2H), 1.98 (s, 3H), 1.85 (m, 2H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 142.6, 127.8, 127.3, 121.1, 120.8, 116.3, 42.3, 27.2, 22.1, 17.1; **MS**-$C_{10}H_{13}N$ (147) m/z (%): 146 (M^+, 100), 132 (43), 117 (19), 91 (12).

2,6-Dimethyl-tetrahydroquinoline (Table 4, entry 6). Light yellow oil, R_f = 0.45 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.73 (d, J = 6.0 Hz, 2H), 6.36 (d, J = 6.0 Hz, 1H), 3.31 (m, 1H), 2.67 (m, 2H), 2.16 (s, 3H), 1.85 (m, 1H), 1.52 (m, 1H), 1.15 (d, J = 6.0 Hz, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 142.4, 129.8, 127.2, 126.2, 121.2, 114.2, 47.3, 30.3, 26.5, 22.6, 20.4; **MS**-$C_{11}H_{15}N$ (161) m/z (%): 161 (M^+, 37), 146 (100), 131 (23), 91 (53).

3-Methyl-tetrahydroquinoline (Table 4, entry 7). Yellow oil, R_f = 0.39 (10% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 6.88 (m, 2H), 6.53 (t, J = 6.0 Hz, 1H), 6.41 (d, J = 9.0 Hz, 1H), 3.18 (m, 1H), 2.73 (t, J = 6.0 Hz, 1H), 2.66 (m, 1H), 2.34 (m, 1H), 1.98 (m, 1H), 0.98 (d, J = 6.0 Hz, 3H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 144.2, 129.5, 126.6, 121.1, 116.9,

113.8, 48.8, 35.4, 27.1, 19.0; **MS**-$C_{10}H_{13}N$ (147) *m*/*z* (%): 147 (M^+, 100), 132 (4), 118 (44), 104 (14), 91 (14).

Tetrahydro-isoquinoline (Table 4, entry 8). Light brown oil, R_f = 0.11 (50% EtOAc in hexane); **^{1}H NMR** (300.128 MHz, $CDCl_3$), δ (ppm) 7.03 (m, 3H), 6.93 (t, J = 6.0 Hz, 1H), 3.93 (s, 2H), 3.06 (t, J = 6.0 Hz, 2H), 2.72 (t, J = 6.0 Hz, 2H), 2.02 (s, 1H); **^{13}C NMR** (75.474 MHz, $CDCl_3$), δ (ppm) 135.8, 134.7, 129.2, 126.1, 125.9, 125.6, 48.2, 43.8, 29.1; **MS**-$C_9H_{11}N$ (133) *m*/*z* (%): 132 (M^+, 100), 117 (12), 104 (80), 78 (18).

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